

## The Heart at High Altitude

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On August 8, 1786 Michel Gabriel Paccard, the village doctor in Chamonix, with his guide Jacques Balmat, made the first ascent of Mont Blanc, and reached a height at which scientific opinion of the day considered life to be insupportable. Since that date the ways in which the body adapts to high altitude have interested in turn the physiologist, the mountaineer, the aviator, and now the cardiologist.

The problem of acclimatization to high altitude is that of adjustment to a diminished atmospheric oxygen tension, which is halved at about 18,000 feet and is reduced to one-third of the pressure at sea level at 27,000 feet, less than the height of Mount Everest. It is remarkable that the human body can tolerate such a wide environmental change.

Several mechanisms are involved in maintaining the oxygen supply to the cells of the body as height is gained, some of which are immediate while others take several days or weeks to reach their full effect. Respiration becomes faster and deeper. This occurs even with 'passive' ascent, as in a decompression chamber or in an aeroplane, and still more so of course when the climb is made on foot. The effect of deeper breathing is to improve alveolar ventilation, so that the alveolar oxygen tension, which is always lower than atmospheric oxygen tension, falls less in proportion than the partial pressure of oxygen in the atmosphere, and the respiratory exchange becomes more efficient. The heart rate quickens and cardiac output increases, at any rate initially, so that more haemoglobin passes through the lungs per minute. The oxygen dissociation curve of haemoglobin is such that a considerable fall in alveolar oxygen tension produces a relatively small percentage drop in haemoglobin oxygen saturation, while in the tissues a small drop in the oxygen tension is accompanied by a large release of oxygen. This effect is further enhanced by a shift of the dissociation curve 'to the left' due to the respiratory alkalosis which follows the loss of carbon dioxide

through overbreathing. If the stay at high altitude is extended the haemoglobin level rises and plasma volume diminishes, thereby increasing the oxygen carrying capacity of the blood by as much as 50 per cent. By these several mechanisms the body is able to maintain an arterial oxygen saturation of over 70 per cent when the atmospheric oxygen tension is halved, and an alveolar/tissue oxygen gradient sufficient to satisfy cell oxygen requirements even during considerable exertion, but at heights greater than 22,000 or 23,000 feet these compensatory adaptations become progressively deficient.

Most people acclimatize to high altitude better when they ascend gradually, and when they undertake physical exertion during the ascent. Gaining height too rapidly especially if accompanied by overexertion during, or soon after the ascent, may lead to acute mountain sickness within a few hours, for reasons that are not well understood.

The effects of high altitude on the heart itself, as distinct from the circulatory adjustments required to tolerate a reduced inspired oxygen tension, are of interest. In the short term the heart rate rises roughly in proportion to the height ascended, though after 'passive' ascent the rise may be delayed a few hours, and the rate falls again as acclimatization to the new altitude develops. Occasionally the response is bradycardia with failure of the pulse to quicken on exercise. The blood pressure usually alters very little either way, and it appears to be dependent on factors other than purely altitude. In the unacclimatized, or when an acclimatized person moves to a higher altitude, the cardiac output has been shown to increase though it is sometimes difficult to discount the effects of exercise; but in residents at 14,900 feet in the Andes the resting cardiac output was found by cardiac catheterization to be within normal limits (Peñaloza *et al.*, 1962), and in acclimatized mountaineers on the Himalayan Scientific Expedition 1960-61 at 19,000 feet normal resting cardiac outputs were found using indirect methods, and the maximum

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output on exercise was 25 per cent lower than at sea level (Pugh, 1962).

Early Himalayan mountaineers believed that the heart dilated at high altitude, presumably because the impulse of an overactive heart could be felt further to the left. X-ray examination has not yet been possible at very great heights, but such radiological evidence as there is at moderate altitude and in the decompression chamber, or very soon after the return from high altitude, lends no support to the view that the heart dilates, nor would one suppose that it should unless it fails.

Anoxia of high altitude, in common with other forms of anoxia, causes pulmonary arteriolar constriction and a rise in pulmonary arterial pressure. This has been demonstrated repeatedly by catheter studies in Andean subjects and in North America. Exercise produces a variable and sometimes disproportionate further rise in pulmonary arterial pressure. This is thought to be the explanation of the sometimes quite severe right-sidedness seen in the electrocardiogram of residents at high altitude, and of the hypertrophy of the right ventricle and muscular pulmonary arteries found at necropsy (Arias-Stella and Saldaña, 1963; Recavarren and Arias-Stella, 1964). Yet, this is not invariably so, and some residents at Morococha in the Andes at 14,900 feet had normal pulmonary arterial pressures. Moreover in a recent study, the writer and his associates (Jackson, Turner, and Ward, 1967), covering 75 per cent of an isolated Himalayan population living between 12,000 and 13,000 feet, found no clinical evidence of pulmonary hypertension, and much less right-sidedness in the electrocardiograms than had been anticipated on the basis of previous South American studies. It is possible that thousands of years of residence at this altitude have resulted genetically in a tolerance of hypoxia of this degree which the North American and many of the Andean people may not have acquired. Unfortunately no catheter studies have yet been possible in resident Himalayan populations.

In visitors to high altitude most evidence points to the complete reversibility of pulmonary hypertension on descending to sea level. In former natives at 14,200 feet, catheterization before and two years after moving to sea level showed a fall in pulmonary arterial pressure to near normal, though not quite (Peñaloza *et al.*, 1962), but as yet there are no post-mortem reports on the hearts and pulmonary vasculature of any of these subjects.

Early studies on the changes in the electrocardiogram due to altitude, notably by Peñaloza and Echevarría (1957) and Peñaloza (1958), were mainly concerned with the changes induced by passive transport of subjects from sea level to near 15,000

feet, and the further modifications during prolonged residence at those heights. Changes at greater altitudes were studied in decompression chambers particularly at centres of aviation medicine because of their importance to flying personnel. Jackson and Davies in 1960 described the electrocardiographic changes in European and Sherpa mountaineers under the very different conditions of difficult climbing with heavy loads to over 19,000 feet on Ama Dablam, and Milledge in 1963 to as high as 24,000 feet on Makalu.

As would be expected, the electrocardiographic changes are in general more pronounced in subjects who have climbed high than in those who have been carried up, but they are similar in character in both groups. The most striking effects are, first, the development of an extreme degree of right axis deviation in the standard limb leads proportional to the height ascended. This is shown as a clockwise rotation of the QRS vector in the frontal plane of as much as 50 degrees, which is greater than can be produced by deep inspiration in a normal subject. Secondly, lowering or inversion of the T wave in right chest leads is found in varying degree in most subjects. It may differ from day to day, but it tends to increase in extent if the stay at high altitude is prolonged for some weeks. These changes are interpreted as being due to right ventricular overload, and possibly myocardial ischaemia, resulting from the increased work the right ventricle has to do in maintaining a normal or increased output of blood of increased viscosity against an augmented pulmonary vascular resistance. Eventually this would be expected to produce right ventricular hypertrophy, with dominant R waves in right chest leads, but this has not yet been seen in visiting mountaineers.

Lowering of the T waves in all leads occurs in some subjects during passive ascent, with recovery of voltage later, and sharp T wave inversion to the left of the transitional zone was seen at 19,000 feet (Jackson and Davies, 1960) for which no satisfactory explanation was available in the absence of symptoms or sequelae, though myocardial ischaemia seems most likely. Atrial or ventricular arrhythmias become more common as with all forms of anoxia, but do not seem important. These changes are not unlike those seen with hypokalaemia. Indeed the rapid rise in the red cell count coupled with increased adrenal cortical activity, and often an increased salt and diminished potassium intake, all act in the direction of potassium depletion of the plasma. Whether these or other electrolyte changes are of sufficient magnitude to influence the electrocardiogram is not yet clearly defined.

It is interesting that similar electrocardiographic

changes to those in climbers going from sea level to very high altitude were seen to develop also in Sherpas normally resident at 12,000 feet who accompanied them to 19,000 feet, none of whom showed the commonly accepted changes of right ventricular hypertrophy in their tracings.

In all cases where the electrocardiogram was repeated after return to sea level it had reverted to normal. The most surprising finding, as Milledge (1963) says, is that the electrocardiogram shows so little evidence of the severe physiological stress imposed at 24,000 feet. It is noteworthy also that the changes described were not accompanied in any subject by recognizable cardiac symptoms.

In recent years acute pulmonary oedema has been diagnosed after a rapid ascent to heights over 11,000 feet, particularly if severe exertion has been undertaken in cold dry air. Houston, a distinguished American mountaineer, was probably the first to demonstrate high altitude pulmonary oedema by chest x-ray film (Houston, 1960), though clinically strong suspicions of the existence of this condition had been raised by the rapid deaths of fit young climbers on high mountains in the Americas and in the Himalayas, usually after a very strenuous day.

The presenting symptoms were increasingly severe dyspnoea, cyanosis, and a productive cough developing in the course of a few hours. A diagnosis of 'fulminating pneumonia' was made by fellow mountaineers who occasionally were doctors. Minor cases may be more frequent than are commonly diagnosed, for many Himalayan climbers have described mild paroxysmal nocturnal dyspnoea, relieved by sitting up or by raising the head and thorax, especially during the early days of an ascent. Indian observers reported a number of cases in soldiers operating on the Tibetan border at heights over 11,000 feet, most of whom were new arrivals and comprised hillsmen as well as plainsmen (Singh *et al.*, 1965). Cases have occurred in acclimatized subjects on reascending to high altitude after a week or two at lower levels. Certain people have been affected on more than one occasion, and the possibility of an idiosyncrasy is raised.

The exact mechanism underlying this condition is unknown. Rapid exposure to high altitude appears to be a necessary factor, with exertion in a cold atmosphere a strong contributory cause. Catheter studies made during attacks by Hultgren and his colleagues (1964) demonstrated the remarkable fact that the pulmonary venous pressure is not raised, thus ruling out left ventricular failure as a cause, and also pulmonary venous constriction which has been postulated. Moreover, post-mortem

examinations have shown no left atrial or left ventricular dilatation or other evidence of left ventricular failure, and in no case has any obvious heart disease been present. The pulmonary arterial pressure, however, was always higher than in any acclimatized residents at 14,000 feet, and it fell after recovery from the attack. It seems that these subjects show excessive anoxic pulmonary arteriolar constriction compared with others, and oxygen inhalation affords striking relief. Increased pulmonary capillary permeability must be involved in the escape of fluid into the air sacs, and it is possible that the continued inhalation of extremely cold, dry air, coupled with anoxia, damages the alveolar walls in some way. High altitude pulmonary oedema is quite unlike the usual forms of acute pulmonary oedema and in some respects resembles the fulminating lung oedema of phosgene gas poisoning. Excessive plasma volume may be a contributory factor, especially in cases occurring after a visit to lower altitudes where a rapid compensatory rise in plasma volume takes place, but basically the mechanism whereby an accession of pulmonary arterial pressure is translated into acute pulmonary oedema remains unexplained.

High altitude pulmonary oedema may be fatal within a few hours, or recovery may be equally rapid, and complete, but recurrences are liable to occur if overexertion and further ascent is undertaken too soon. Death during an attack has been sufficiently frequent for it to be an important hazard which mountaineers, both medical and non-medical, should know how to treat. Oxygen inhalation is the most important measure, though deaths have occurred despite its use. A rapidly acting diuretic should be given if available, and the patient moved to a lower level wherever possible. Morphine may be valuable in relieving dyspnoea and allaying anxiety, but the rationale for giving digoxin is doubtful, and benefit from its use has been denied.

Little is known about many of the other interesting problems relating to the heart and heart disease at high altitudes. Persistence for several years after birth of the physiological elevation of the pulmonary arterial pressure in the newborn has been reported in the Andes (Peñaloza *et al.*, 1962), where also there is a considerably higher incidence of patent ductus arteriosus and of the Eisenmenger syndrome in children, and an unusual number of cases of pulmonary hypertension were found in children at Leadville situated at 10,150 feet in the Rocky Mountains (Vogel *et al.*, 1962). Yet experiences in the Himalayas, albeit involving smaller populations, do not support these findings, and care may be needed in assuming that conclusions arrived at in one part of the world can be applied

to basically different ethnic groups in the other hemisphere.

Knowledge about the incidence of coronary artery disease in peoples living at great heights is scanty, partly because there are so few living permanently at over 10,000 feet, with the exception of Tibet where entry is impossible, but there is some evidence that ischaemic heart disease is less common in them than in Western communities. In two Himalayan surveys symptoms of angina were rare, electrocardiographic evidence of ischaemic heart disease was conspicuous by its infrequency, and serum cholesterol levels were low. Such studies, however, have covered too small numbers for firm conclusions to be drawn, and more detailed surveys with better technical and laboratory facilities are needed.

It has been postulated that excursions to high altitude involving sustained physical exertion promote the development of inter-coronary anastomoses in the heart. Proof of this is lacking, and would probably require very detailed serial coronary angiography, while caution is required in applying the results of animal experimentation to man because of differences in the design of the coronary vasculature in different species.

No discussion of this subject is complete without some mention of the risks to patients with heart disease involved in travelling by air. All modern aircraft have pressurized cabins, so that regardless of the height at which the aircraft flies the pressure in the cabin rarely falls below that met with in ascending to a height of 5000 or 6000 feet. Most people, including invalids, can tolerate this slight reduction in the inspired oxygen tension without discomfort; but where the cardiac status is precarious, especially in heart failure, or with severe angina and with some arrhythmias, oxygen can and should be supplied with an oxygen mask from the moment of take-off. On the whole, cardiac patients tolerate

air travel well unless they are severely dyspnoeic, and many find the strain of flying less than that of a long journey involving tiring changes from ships to trains and cars or vice versa.

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